# WEST Search History

Hide Items Restore Clear Cancel

DATE: Monday, May 23, 2005

| Hide? | Set Name | Query | Hit Count |
|---|---|---|---|
| | | *DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=AND* | |
| ☐ | L1 | (clfa or clf-a or fnbp or fn-bp or (clumping near2 factor)).clm. | 15 |
| ☐ | L2 | anticlfa or anti-clfa or anti-clf-a or anticlumping or anti-clumping (antibod$ near5 clumping near5 factor) | 61 |
| ☐ | L3 | L2 not l1 | 60 |
| ☐ | L4 | anticlfa or anti-clfa or anti-clf-a or anticlumping or anti-clumping or (antibod$ near5 clumping near5 factor) | 184 |
| ☐ | L5 | L4 not l1 | 179 |
| ☐ | L6 | l5 and (staph$ or aureus or epidermidis) | 12 |
| ☐ | L7 | l6 and (human or sapian or man) | 8 |
| ☐ | L8 | l7 and (mammal or human) | 8 |

END OF SEARCH HISTORY

Updated Search 5/05

First Hit Fwd Refs

L1: Entry 11 of 15 File: USPT Feb 17, 2004

US-PAT-NO: 6692739
DOCUMENT-IDENTIFIER: US 6692739 B1

TITLE: Staphylococcal immunotherapeutics via donor selection and donor stimulation

DATE-ISSUED: February 17, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Patti; Joseph M. | Cumming | GA | | |
| Foster; Timothy J. | Dublin | | | IE |
| Hook; Magnus | Houston | TX | | |


US-CL-CURRENT: 424/130.1; 424/137.1, 424/150.1, 424/185.1, 530/387.1, 530/387.5, 530/388.2, 530/388.4

CLAIMS:

What is claimed is:

1. A selected purified human donor immunoglobulin composition comprising an antibody titer to an S. aureus serine-aspartate repeat (Sdr) protein in combination with an antibody titer to an S. epidermidis serine-asparate repeat (Sdr) protein wherein both antibody titers are higher than that found in pooled intravenous immunoglobulin obtained from unselected human donors, said composition obtained by a method comprising obtaining blood or plasma samples from human donors, screening said samples so as to select those samples having an antibody titer to an S. aureus Sdr protein and an antibody titer an S. epidermidis Sdr protein that are both in an amount that is higher than that found in pooled intravenous immumoglobulin obtained from unselected donors, recovering blood or plasma from the selected high-titer donors, and treating the donor blood plasma to obtain immumoglobulin in a purified state having an antibody titer to an S. aureus Sdr protein and an antibody titer to an S. epidermidis Sdr protein that are both in an amount which is higher than that found in pooled intravenous immunoglobulin obtained from unselected human donors.

2. The door immunoglobulin composition of claim 1 wherein the S. aureus Sdr protein is selected from the group consisting of clumping factor A (ClfA), clumping factor B (ClfB), SdrC, SdrD, and SdrE.

3. The donor immunoglobulin composition of claim 1 wherein the S. epidermidis Sdr protein is selected from the group consisting of SdrF, SdrG and SdrH.

4. The donor immunoglobulin composition of claim 1 wherein the S. aureus Sdr protein is clumping factor A (ClfA).

5. The donor immunoglobulin composition of claim 1 wherein the S. aureus Sdr protein is clumping factor B (ClfB).

6. The donor immunoglobulin composition of claim 1 wherein the S. aureus Sdr protein is SdrC.

7. The donor immumoglobulin composition of claim 1 wherein the S. aureus Sdr protein is SdrD.

8. The donor immumoglobulin composition of claim 1 wherein the S. epidermidis Sdr protein is SdrE.

9. The donor immunoglobulin composition of claim 1 wherein the S. epidermidis Sdr protein is SdrF.

10. The donor immunoglobulin composition of claim 1 wherein the S. epidermidis Sdr protein is SdrG.

11. The donor immunoglobulin composition of claim 1 wherein the S. epidermidis Sdr proten is SdrH.

12. The donor immunoglobulin composition of claim 1 wherein the composition has an antibody titer to an S. aureus Sdr protein in an amount that is 2-fold or greater than that found in pooled intravenous immunoglobulin obtain from unselected donors.

13. The donor immunoglobulin composition of claim 1 wherein the composition has a total antibody titer to an S. aureus Sdr protein that is greater than 0.2 Units/mg/lgG.

14. A purified human donor immunoglobulin composition comprising an antibody titer to an S. aureus serine-aspartate repeat (Sdr) protein combination with an antibody titer to an S. epidermidis serine-aspartate repeat (Sdr) protein wherein both antibody titers are higher than that found in pooled intravenous immunoglobulin obtained from unselected human donors obtained by a method comprising administering an S. aureus Sdr protein to a human host donor in an amount sufficient to induce an antibody titer to the S. sureus Sdr protein that is higher that found in pooled intravenous immunoglobulin obtained from unselected donors, and administering an S. epidermidis Sdr protein to a human host donor in an amount sufficient to induce an antibody titer to the S. epidermidis Sdr protein that is higher than that found in pooled intravenous immumoglobulin obtained from unselected donors, recovering blood or plasma samples from the induced donors, and treating the donor blood or plasma to obtain immunogloubulin in a purified state having antibody titer to an S. aureus Sdr protein and an antibody titer to an S. epidermidis Sdr protein that are both in an amount which is higher than that found in pooled intravenous immunoglobulin obtained from unselected human donors.

15. The donor immunoglobulin composition of claim 14 wherein the S. aureus Sdr protein is selected from the group consisting of clumping factor A (ClfA), clumping factor B (ClfB), SdrC, SdrD, and SdrE.

16. The donor immunoglobulin composition of claim 14 wherein the S. epidermidis Sdr protein is selected from the group consisting of SdrF, SdrG and SdrH.

17. The donor immunoglobulin composition of claim 14 wherein the S. aureus Sdr protein is clumping factor A (ClfA).

18. The donor immunoglobulin composition of claim 14 wherein the S. aureus Sdr protein is clumping factor B (ClfB).

19. The donor immunoglobulin composition of claim 14 wherein the S. aureus Sdr protein is SdrC.

20. The donor immunoglobulin composition of claim 14 wherein the S. aureus Sdr protein is SdrD.

21. The donor immunoglobulin composition of claim 14 wherein the S. aureus Sdr protein is SdrE.

22. The donor immunoglobulin composition of claim 14 wherein the S. epidermidis Sdr protein is SdrF.

23. The donor immunoglobulin composition of claim 14 wherein the S. epidermidis Sdr protein is SdrG.

24. The donor immunoglobulin composition of claim 14 wherein the S. episermidis Sdr protein is SdrH.

25. The donor immunoglobulin composition of claim 14 wherein the composition has an antibody titer to an S. areus Sdr protein in an amount that is 2-fold or greater than that found in pooled intravenous immunoglobulin obtain from unselected donors.

26. The donor immunoglobulin composition of claim 14 wherein the composition has a total antibody titer to an S. aureus Sdr protein that is greater than 0.2 Units/mg/lgG.

| Search | Most Recent Queries | Time | Resu |
|---|---|---|---|
| #30 | **Related Articles** for **PubMed** (Select **10456895**) | 15:18:04 | 1 |
| #28 | **Related Articles** for **PubMed** (Select **2744851**) | 15:17:33 | 1 |
| #25 | **Related Articles** for **PubMed** (Select **1943852**) | 15:12:54 | 1 |
| #19 | **Related Articles** for **PubMed** (Select **10618270**) | 15:10:42 | 4 |
| #17 | **Related Articles** for **PubMed** (Select **14638774**) | 15:07:36 | 5 |
| #16 | Search **human immunotherapy staphylococcus fibrinogen** | 15:05:37 | |
| #15 | Search **human immunotherapy staphylococcus** | | |

Zentralbl Bakteriol. 1994 Nov;281(4):495-501. 

**Role of antibodies against fibronectin-, collagen-binding proteins and alphatoxin in experimental Staphylococcus aureus peritonitis and septicaemia in neutropenic mice.**

**Rozalska B, Wadstrom T.**

Department of Medical Microbiology, University of Lund, Sweden.

We have investigated the protective role of hyperimmune rabbit IgG against two surface structures of Staphylococcus aureus, i.e. fibronectin-, and collagen-binding proteins as well as alpha-toxin in experimental peritonitis and septicaemia in neutropenic mice pretreated with cyclophosphamide. This treatment markedly decreased clearance of bacteria from mouse organs. With combined immunotherapy given passively bacteria were eradicated more efficiently for all animals sampled, comparative to controls.

PMID: 7727897 [PubMed - indexed for MEDLINE]

J Med Microbiol. 1994 Feb;40(2):79-89. Related Articles, Links

# Virulence factors involved in the pathogenesis of bovine intramammary infections due to Staphylococcus aureus.

**Sutra L, Poutrel B.**

Faculte des Sciences, Universite d'Angers.

Staphylococcus aureus is a major causative agent of intramammary infections in dairy cows. In this report, the pathogenesis of these infections is described. The potential role in virulence of S. aureus surface components (adhesins, protein A and capsular polysaccharides), toxins, extracellular enzymes and coagulase, and perspectives for the development of an efficient vaccine are discussed.

Publication Types:
- Review

PMID: 8107066 [PubMed - indexed for MEDLINE]

Scand J Immunol. 1993 May;37(5):575-80. Related Articles, Links

## Protective opsonic activity of antibodies against fibronectin-binding proteins (FnBPs) of Staphylococcus aureus.

**Rozalska B, Wadstrom T.**

Department of Medical Microbiology, University of Lund, Sweden.

In this report, opsonic activity of hyperimmune rabbit IgG against fibronectin-binding proteins (gal-FnBP A and ZZ-FnBP B) of Staphylococcus aureus is described. Moreover, the action of IgG purified from serum of rabbits immunized with 'combined vaccine' (fibronectin-binding protein A+collagen-binding protein+alpha-toxoid) is shown. The opsonic activity has been studied in an in vitro phagocytosis assay as well as in vivo. Mice which had been infected intraperitoneally with S. aureus strain Cowan 1 pretreated (opsonized in vitro) with specific anti-FnBPs IgG were able to eliminate the staphylococci from the peritoneal cavity and liver more rapidly than controls. Also, clearance from the bloodstream of intravenously injected S. aureus Cowan 1 as well as S. aureus U320, opsonized with IgG anti-FnBPs or anti-FnBP+CnBP+alpha-toxoid, was more effective than observed in control groups. In other in vivo experiments it was shown that mice passively immunized with hyperimmune IgG anti-FnBP (one or two doses, intravenously) before challenge with S. aureus Cowan I eliminated the bacteria better than controls injected only with preimmune IgG.

PMID: 8484103 [PubMed - indexed for MEDLINE]

J Biol Chem. 1998 May 22;273(21):13177-81. 

# Multiple binding sites in the interaction between an extracellular fibrinogen-binding protein from Staphylococcus aureus and fibrinogen.

**Palma M, Wade D, Flock M, Flock JI.**

Department of Immunology, Microbiology, Pathology, and Infectious Diseases, Karolinska Institutet, Huddinge University Hospital, F82, Sweden.

Efb (previously Fib) is a fibrinogen-binding protein secreted by Staphylococcus aureus. It has previously been shown that it plays a role in a wound infection model in the rat and that antibodies against Efb reduce the number of recovered bacteria from the mammary glands in a mouse mastitis model. Efb binds to the alpha-chain of fibrinogen and does not participate in bacterial adherence to fibrinogen. The binding of Efb to fibrinogen is divalent,.with one binding site within the two repeat regions in Efb at the N terminus and one binding site at the C terminus. The divalent binding nature leads to precipitation of Efb-fibrinogen complex when the proteins are added to each other at a 1:1 molar ratio. The interaction between Efb and fibrinogen is strongly enhanced by Ca2+ or Zn2+ but not by Mg2.

PMID: 9582359 [PubMed - indexed for MEDLINE]

Mol Microbiol. 1997 Sep;25(6):1065-76. Related Articles, Links

# The dipeptide repeat region of the fibrinogen-binding protein (clumping factor) is required for functional expression of the fibrinogen-binding domain on the Staphylococcus aureus cell surface.

**Hartford O, Francois P, Vaudaux P, Foster TJ.**

Department of Microbiology, Moyne Institute of Preventive Medicine, Trinity College, Dublin, Ireland.

Clumping factor of Staphylococcus aureus is a fibrinogen-binding protein that is located on the bacterial cell surface. The protein has an unusual repeat domain (region R) comprising mainly the dipeptide aspartate and serine. To determine if region R has a role in the surface display of the fibrinogen-binding region A domain, deletions lacking the region R encoding region of the clfA gene were generated. To determine the minimum length of region R required for wild-type levels of ClfA expression, variants with truncated region R domains were constructed. S. aureus cells expressing mutated clfA genes were tested for (i) proteins released by lysostaphin treatment that reacted with antisera specific for region A, (ii) clumping in soluble fibrinogen, (iii) adherence to immobilized fibrinogen and (iv) expression of the ClfA antigen on the cell surface by fluorescent activated cell sorting analysis. Each construct expressed three major immunoreactive proteins, two of which were putative N-terminal degradation products. Region R residues greater than 40 were required between region A and W (72 residues between region A and the LPDTG sorting signal) for wild-type levels of clumping in fibrinogen. A stepwise decrease in clumping titre was observed as the distance between region A and LPDTG was decreased from 72 to 4 residues. Similarly, a decrease in binding of anti-ClfA serum and in binding to fibrinogen-coated plastic surfaces was observed with cells expressing ClfA with 40 region R residues or less. Nevertheless, low levels of adherence to fibrinogen and binding to anti-ClfA serum occurred with ClfA derivatives that lacked region R altogether. This indicates that a small proportion of the ClfA molecules are linked to peptidoglycan very close to the cell surface but that residues greater than 72 are needed to allow sufficient ClfA molecules to span the entire cell wall and to display the biologically active A domain in a form that can participate fully in fibrinogen binding.

Mol Microbiol. 1995 Jun;16(5):895-907. 

# Identification of the ligand-binding domain of the surface-located fibrinogen receptor (clumping factor) of Staphylococcus aureus.

**McDevitt D, Francois P, Vaudaux P, Foster TJ.**

Department of Microbiology, Moyne Institute, Trinity College, Dublin, Ireland.

The ability of Staphylococcus aureus to bind to fibrinogen and fibrin is believed to be an important factor in the initiation of foreign-body and wound infections. Recently, we reported the cloning and sequencing of the gene clfA encoding the fibrinogen receptor (clumping factor, ClfA) of S. aureus strain Newman and showed that the gene product was responsible for the clumping of bacteria in soluble fibrinogen and for the adherence of bacteria to solid-phase fibrinogen. This was confirmed here by showing that antibodies raised against purified Region A inhibited both of these properties. Also, immunofluorescent microscopic analysis of wild-type Newman and a clfA::Tn917 mutant of Newman with anti-ClfA Region A sera confirmed that Region A is exposed on the bacterial cell surface. Furthermore, polystyrene beads coated with the Region A protein formed clumps in soluble fibrinogen showing that the ClfA protein alone is sufficient for the clumping phenotype. Western immunoblotting with anti-ClfA Region A antibodies identified the native ClfA receptor as a 185 kDa protein that was released from the cell wall of S. aureus by lysostaphin treatment. A single extensive ligand-binding site was located within Region A of the ClfA protein. Truncated ClfA proteins were expressed in Escherichia coli. Lysates of E. coli and proteins that had been purified by affinity chromatography were tested for (i) their ability to bind fibrinogen in Western ligand blotting experiments, (ii) for their ability to inhibit clumping of bacteria in fibrinogen solution and adherence of bacteria to solid-phase fibrinogen, and (iii) for their ability to neutralize the blocking activity of anti-ClfA Region A antibody. These tests allowed the ligand-binding domain to be localized to a 218-residue segment (residues 332-550) within Region A.

PMID: 7476187 [PubMed - indexed for MEDLINE]

FEMS Immunol Med Microbiol. 1994 Nov;10(1):47-53. Related Articles, Links

**Vaccination with Staphylococcus aureus fibrinogen binding proteins (FgBPs) reduces colonisation of S. aureus in a mouse mastitis model.**

**Mamo W, Boden M, Flock JI.**

Swedish University of Agricultural Sciences, Department of Veterinary Microbiology, Uppsala.

A mouse mastitis model was used to study the effect of vaccination with fibrinogen binding proteins and collagen binding protein from Staphylococcus aureus against challenge infection with S. aureus. The mice vaccinated with fibrinogen binding proteins showed reduced rates of mastitis compared with controls. Gross examination of challenged mammary glands of mice showed that the glands of mice immunized with fibrinogen binding proteins developed mild intramammary infection or had no pathological changes compared with glands from control mice. Histopathological examination of tissue sections from challenged glands showed that most glands from mice vaccinated with fibrinogen binding protein developed disseminated necrosis or had no pathological changes. A significantly reduced number of bacteria could be recovered in the glands from mice immunized with fibrinogen binding proteins as compared with controls. In a similar study, immunization of mice with collagen binding protein did not induce protection against challenge infection with S. aureus.

PMID: 7874078 [PubMed - indexed for MEDLINE]

Foster

DOCUMENT-IDENTIFIER: US 6008341 A
TITLE: S. aureus fibrinogen binding protein gene

Abstract Text (1):
The isolation of the S. aureus fibrinogen binding protein gene is described and a minimal fibrinogen binding protein is identified. The protein finds use as a vaccine or a pharmaceutical composition for application to prevent infection, promotion of wound healing, blocking adherence to indwelling medical devices, or diagnosis of infection.

Brief Summary Text (2):
The invention relates to the isolation of the fibrinogen binding protein gene from Staphylococcus aureus and to the use of the fibrinogen binding protein and antibodies generated against it for wound healing, blocking adherence to indwelling medical devices, immunisation or diagnosis of infection.

Brief Summary Text (4):
In hospitalised patents Staphylococcus aureus is an important cause of infections associated with indwelling medical devices such as catheters and prostheses (Maki, 1982; Kristinsson, 1989) and non-device related infections of surgical wounds. A recent significant increase in isolates from European and U.S. hospitals which are resistant to several antibiotics and the potential threat of emergence of vancomycin resistance in S. aureus has reinforced the importance of developing alternative prophylactic or vaccine strategies to decrease the risk of nosocomial infections due to S. aureus.

Brief Summary Text (5):
Initial localised infections can lead to more serious invasive infections such as septicaemia and endocarditis. In infections associated with medical devices, plastic and metal surfaces become coated with host plasma and matrix proteins such as fibrinogen and fibronectin shortly after implantation (Baier, 1977; Kochwa et al, 1977; Cottonaro et al, 1981). The ability of S. aureus to adhere to these proteins is believed to be a crucial determinant for initiating infection (Vaudaux et al, 1989, 1993). Vascular grafts, intravenous catheters, artificial heart valves and cardiac assist devices are thrombogenic and are prone to bacterial colonization. S. aureus is the most damaging pathogen of such infections.

Brief Summary Text (6):
Fibrin is the major component of blood clots and fibrinogen/fibrin is one of the major plasma proteins deposited on implanted biomaterial. There is considerable evidence that bacterial adherence to fibrinogen/fibrin is of importance in initiation of device related infection. (i) S. aureus adheres to plastic coverslips coated in vitro with fibrinogen in a dose-dependent manner (Vaudaux et al, 1989) and to catheters coated in vitro with fibrinogen (Cheung and Fischetti, 1990). (ii) The organism binds avidly via a fibrinogen bridge to platelets adhering to surfaces in a model that mimics a blood clot or damage to a heart valve (Herrmann et al., 1993). (iii) S. aureus can adhere to cultured endothelial cells via fibrinogen deposited from plasma acting as a bridge (Cheung et al., 1991). This suggests that fibrinogen could have a direct role in promoting invasive endocarditis. (iv) Mutants defective in a global regulatory gene sar have reduced adherence to fibrinogen and have reduced infectivity in a rat endocarditis infection model (Cheung et al., 1994). While this is indicative of a role for adherence to fibrinogen in initiating endocarditis it is by no means conclusive because sar mutants are pleiotropic and could also lack other relevant factors.

Brief Summary Text (7):
A receptor for fibrinogen often called the "clumping factor" is located on the surface of S. aureus cells (Hawiger et al., 1978, 1982). The interaction between bacteria and fibrinogen in solution results in instantaneous clumping of bacterial cells. The binding site for clumping factor of fibrinogen is located in

the C-terminus of the gamma chain of the dimeric glycoprotein. The affinity for the fibrinogen receptor is very high (Kd 9.6.times.10.sup.-9 M) and clumping occurs in low concentrations of fibrinogen. It is assumed that clumping factor also promotes bacterial adhesion to solid-phase fibrinogen and to fibrin.

Brief Summary Text (9):
More recently it has been shown that S. aureus releases several proteins that can bind to fibrinogen (Boden and Flock, 1989, 1992, 1994; Homonylo McGavin et al., 1993). One of these is probably the same as the broad spectrum ligand binding protein identified by Homonylo McGavin et al., (1993). Another is coagulase (Boden and Flock, 1989), a predominately extracellular protein that activates the plasma clotting activity of prothrombin. Coagulase binds prothrombin at its N-terminus and also interacts with fibrinogen at its C-terminus (McDevitt et al., 1992). However, a hypothesis that the cell-bound form of coagulase is the clumping factor was disproved when coagulase-defective mutants were shown to retain clumping factor activity (McDevitt et al., 1992). There is no evidence that the fibrinogen binding region of any of these proteins is exposed on the bacterial cell surface and consequently there is no evidence that any is clumping factor.

Brief Summary Text (13):
The present invention relates to an isolated fibrinogen binding protein gene from S. aureus, particularly the DNA molecule having the sequence shown in FIG. 2 and Sequence ID NO.1, or a substantially similar sequence also encoding S. aureus fibrinogen binding protein.

Brief Summary Text (14):
The invention also relates to hybrid DNA molecules, e.g. plasmids comprising a nucleotide sequence coding for said protein. Further the invention relates to transformed host micro-organisms comprising said molecules and their use in producing said protein. The invention also provides antisera raised against the above fibrinogen binding protein and vaccines or other pharmaceutical compositions comprising the S. aureus fibrinogen binding protein. Furthermore the invention provides diagnostic kits comprising a DNA molecule as defined above, the S. aureus fibrinogen binding protein and antisera raised against it.

Drawing Description Text (3):
FIG. 1. Adherence of S. aureus Newman strains to fibrinogen-coated PMMA coverslips. The number of adherent bacteria is shown as a function of fibrinogen adsorbed on the coverslip. The symbol for Newman wild type is IIIIXIII. Symbols for Newman mutant strains are as follows: mutant 1, -.quadrature.-; mutant 2 ,-.DELTA.-; mutant 3, -.diamond.-; mutant 4, -.gradient.-. Symbols for Newman mutants carrying pCF16 are as follows: mutant 1,-.box-solid.-; mutant 2,-.tangle-solidup.-; mutant 3,-.diamond-solid.-; mutant 4,-.tangle-soliddn.-.: The number of bacterial cells bound is shown as CFU (mean+/-range, n=2). In points where range bars are not visible, the bars are smaller than the symbols.

Drawing Description Text (4):
FIG. 2. (A) Nucleotide and deduced amino acid sequence of the clfA gene of Staphylococcus aureus strain Newman. The sequence has been lodged in the EMBL Data Library under the accession number Z18852 SAUCF. Putative -35, -10, ribosome binding site (RBS) and transcriptional stop regions are indicated on the nucleotide sequence. For the ClfA protein, the start of the signal peptide (S), non repeat region (A), repeat region (R), wall-spanning region (W) and membrane spanning region (M) are indicated by horizontal arrows. The LPXTG motif is underlined.

Drawing Description Text (8):
FIG. 5. Inhibition of adherence of strain Newman .DELTA.spa to fibrinogen-coated PMMA coverslips by anti-ClfA sera and preimmune sera. The symbol for anti Region A serum N2 is -.box-solid.- and the symbol for preimmune serum N2 is -.quadrature.-. The symbol for anti Region RWM serum C2 is -

.circle-solid.-. The percentage inhibition is shown as mean+/-range, n=2. In points where range bars are not visible, the bars are smaller than the symbols.

Drawing Description Text (10):
FIG. 7. (A) Inhibition of adherence of S. aureus Newman to fibrinogen-coated coverslips by lysates containing ClfA truncates. Symbols are E. coli pCF24 uninduced lysate -.DELTA.-, E. coli pCF24 induced lysate -.tangle-solidup.- E. coli pCF25 uninduced lysate -.quadrature.-, E. coli pCF25 induced lysate -.box-solid.-. The percentage inhibition is shown as mean+/-range, n=2. In points where range bars are not visible, the bars are smaller than the symbols.

Drawing Description Text (11):
(B) Inhibition of adherence of S. aureus Newman to fibrinogen-coated coverslips by lysates containing ClfA truncates. Symbols are E. coli pCF27 lysate -.box-solid.-, E. coli pCF28 lysate -.circle-solid.-, E. coli pCF29 lysate -.tangle-solidup.-, E. coli pCF30 lysate -.tangle-soliddn.- , E. coli pCF31 lysate -.diamond-solid.-. The percentage inhibition is shown as mean+/-range, n=2. In points where range bars are not visible, the bars are smaller than the symbols.

Drawing Description Text (12):
FIG. 8. Western immunoblotting of ClfA proteins. Proteins released from the cell wall of S. aureus strains Newman (lane 3) and Newman clfA (lane 4), and proteins expressed by E. coli TBl pCF3 (carrying the cloned clfA gene, lane 2) and by E. coli TBl without the plasmid (lane 1), were studied by Western immunoblotting with anti-ClfA antibodies. Approximately 100 micro g of protein was loaded for each sample. Sizes are in kDa.

Drawing Description Text (13):
FIG. 9. S. aureus strains were studied by immunofluorescence with anti-ClfA N2 serum.
Newman .DELTA.spa::Tc.sup.r cells (+) and Newman .DELTA.spa::Tc.sup.r clfA::Tn917 cells (-).

Drawing Description Text (14):
FIG. 10. Adherence of S. aureus Newman strains to PMMA coverslips coated in vitro with fibrinogen. The number of adherent bacteria is shown as a function of fibrinogen adsorbed on the coverslip. The symbols are, Newman wild type, -.smallcircle.-; Newman clfA::Tn917, -.circle-solid.-. The number of bacterial cells bound is shown as c.f.u. (mean+/-range, n=2). In points where range bars are not visible, the bars are smaller than the symbols.

Drawing Description Text (15):
FIG. 11. Adherence of S. aureus Newman strains onto segments of ex vivo polymer tubing exposed to canine blood. Adherence was tested to both ex vivo polyvinylchloride (PVC) and to ex vivo polyethylene (PE). The symbols are, Newman wild type, -.smallcircle.-; Newman clfA::Tn917, -.circle-solid.-. The number of bacterial cells bound is shown as c.f.u. (mean+/-range, n=2). In points where range bars are not visible, the bars are smaller than the symbols.

Drawing Description Text (16):
FIG. 12. Adherence of S. aureus 8325-4 strains onto segments of ex vivo polymer tubing exposed to canine blood. Adherence was tested to both ex vivo polyvinylchloride (PVC) and to ex vivo polyethylene (PE). The symbols are: 8325-4 wild type, -.quadrature.-; 83254 clfA::Tn917, -.box-solid.-; 8325-4 clfA::Tn917 (pCF4), . The number of bacterial cells bound is shown as c.f.u. (mean=/-range, n=2). In points where range bars are not visible, the bars are smaller than the symbols.

Detailed Description Text (3):
Transposon Tn917 (Tomich et al., 1980) was used to generate insertion mutants that eliminated the

fibrinogen clumping phenotype of S. aureus strain Newman. The temperature sensitive plasmid pTV1ts which carries Tn917 (Youngman, 1985) was transferred into strain Newman and several transposon insertion banks were isolated by growing cultures at 43.degree. in broth containing erythromycin (to select for Tn917 after plasmid elimination). Cultures of the banks were mixed with fibrinogen, the agglutinated cells were removed and the surviving cells in the supernatants were screened for clumping factor-deficient mutants. Four mutants were isolated from separate banks. The Tn917 elements were transduced into a wild-type Newman host with phage 85. In each case all the transductants screened had inherited the clumping factor deficiency proving that the Tn917 insertions caused the mutant phenotypes. The clumping factor mutants expressed the same level of coagulase as the wild-type strain, further supporting the conclusion that clumping factor and coagulase are distinct entities.

Detailed Description Text (5):
The 7 kb HindIII fragment was subcloned into pCL84, a single copy non-replicating vector which integrates into the chromosome of S. aureus (Lee et al., 1991), forming pCF16. pCF16 was transformed into S. aureus strain CYL316 (Lee et al., 1991) selecting for tetracycline resistance. The integrated plasmid was then transduced with phage 85 into each of the Newman clf mutants. In a microtitre clumping assay the Newman mutants were completely devoid of activity even at the highest concentrations of fibrinogen, whereas the wild-type had a titre of 2048 and could interact productively with very low concentrations of fibrinogen. The integrated single copy plasmid pCF16 restored the clumping activity of each of the mutants to the same level as that of the parental strain. Thus the HindIII fragment must express a functional protein which complements the clumping deficiency of the mutants.

Detailed Description Text (6):
S. aureus Newman adhered to solid-phase fibrinogen coated onto polymethylmethacrylate (PMMA) coverslips in a concentration dependent manner (FIG. 1). Each clf mutant showed drastic reduction in adherence. This was restored to the level of the parental strain by pCF16. This data shows that the ability of Newman to form clumps in soluble fibrinogen correlates with bacterial adherence to solid-phase fibrinogen.

Detailed Description Text (8):
It is not obvious from the primary structure of ClfA or by comparison of ClfA with other ligand binding proteins of S. aureus (fibronectin binding protein, Signas et al., 1989; collagen binding protein, Patti et al., 1992) which part of ClfA interacts with fibrinogen.

Detailed Description Text (13):
A rabbit was immunised with 30 micro g of a mixture of the 105 kDa, 75 kDa, 55 kDa and 42 kDa proteins along with Freund's complete adjuvant. The immune sera was called N2. One rabbit was also immunised with 18 micro g of the purified 42 kDa ClfA truncate and the immune serum for this was called N3. Bacterial interaction with fibrinogen can be measured by a quantitative clumping titration assay (Switalski, 1976). In this assay, doubling dilutions of a fibrinogen solution (1 mg/ml) are mixed in a microtitre dish with a suspension of 2.times.10.sup.7 cells for 5 min with gentle shaking. A standard clumping concentration of fibrinogen was defined as 2.times. the titre. To this was added varying amounts of the anti-ClfA serum to measure the minimum inhibitory concentration that stops the clumping reaction (Table 2). Both N2 and N3 sera were potent inhibitors of the clumping of bacteria. Preimmune sera did not inhibit the clumping of bacteria. N2 sera also had a potent inhibitory activity on bacterial adhesion to surface-bound fibrinogen in the coverslip assay (McDevitt et al., 1992, 1994), expressing 95% inhibition at 1 micro g protein/ml (FIG. 5). Preimmune sera did not have any inhibitory activity even at a protein concentration of 100 micro g/ml (FIG. 5). In addition, antisera raised against regions R, W and M (C2) (see section 4 below) failed to inhibit adherence even at 100 micro g/ml (FIG. 5).

Detailed Description Text (18):
An antibody neutralisation assay was adopted to help localise further the active site within residues 221-550. This assay was conducted with a protein A negative deletion mutant of S. aureus strain Newman (Patel et al., 1987) to prevent non specific reaction with IgG. Polyclonal antibodies raised against the A region of ClfA (N2) inhibited the clumping of bacteria in soluble fibrinogen (see section 2 above). In the standard clumping assay with the clumping concentration at 2.times. the titre, the concentration of lysates that blocked the inhibitory activity of 4.68 micro g of serum (2.times. the inhibitory concentration, Table 2) was determined. The lysates containing ClfA fusion proteins were assayed for their ability to neutralise the inhibiting activity of the antibodies. Truncates containing the active site might be able to adsorb out antibodies generated against the active site and thus neutralise the blocking effect on cell clumping. The lysates containing proteins expressed by pCF24 and pCF31 neutralised the inhibiting activity of the antibodies while a lysate containing the fusion protein expressed by pCF25 (Region R,W and M) did not inhibit (Table 4). Lysates containing small fusion proteins expressed by pCF30 were able to neutralise the inhibiting activity of antibodies while lysates containing fusion proteins expressed by pCF27 and pCF29 had no such activity (Table 4). Taken together this suggested that the active site is located in a 218 residue region between residues 332 and 550.

Detailed Description Text (22):
Proteins released from the cell wall of S. aureus strains and a lysate of E. coli expressing the cloned clfA gene were studied by Western immunoblotting with anti ClfA antibodies in order to identify ClfA protein(s). A lysate of E. coli TB1 (pCF3) (carrying the cloned clfA gene) contained several immunoreactive proteins (FIG. 8, lane 2). The largest of these was ca. 190 kDa. The smaller proteins are probably derivatives caused by proteolysis. S. aureus strain Newman also expresses a ca. 190 kDa immunoreactive protein (FIG. 8, lane 3). A smaller immunoreactive protein of ca. 130 kDa was also detected and is probably also caused by proteolysis. Despite the presence of protease inhibitors and studying proteins released from cells harvested at different stages in the growth cycle (from mid-exponential to late stationary), two proteins of these sizes were always present (data not shown). Both proteins were absent in extracts of the clumping factor negative transposon insertion mutant of Newman (FIG. 8, lane 4) indicating that they are products of the clfA gene.

Detailed Description Text (23):
Previously we reported the size of the ClfA protein to be ca. 130 kDa (McDevitt et al., 1994) in an affinity blotting assay with fibrinogen and peroxidase labelled anti-fibrinogen antibodies. Our current immunoblotting assay is much more sensitive than the affinity blotting assay. In addition, we now know that the ClfA protein is very sensitive to degradation. Indeed the predominant immunoreactive protein detected in samples from both E. coli TB1 (pCF3) and S. aureus strain Newman which have been frozen and thawed more than twice is 130 kDa indicating that the ca. 190 kDa protein is labile (data not shown). Thus, the ca. 130 kDa protein detected in the affinity blotting assay is most probably a smaller derivative of ClfA. The apparent size of the native ClfA protein of strain Newman appears to be ca. 190 kDa. This is double that predicted from the DNA sequence, but this might be due to the unusual structure and is consistent with the aberrantly high apparent molecular weight of recombinant proteins (Table 1). The recombinant N-terminal Region A protein expressed by E. coli pCF17 also had an unexpectedly high apparent molecular weight.

Detailed Description Text (25):
Anti-ClfA region A sera (N2) was used to confirm that Region A of ClfA is exposed on the bacterial cell surface. Protein A-deficient mutants of Newman and Newman clfA::Tn917 (clumping factor transposon insertion mutant) were isolated by transducing the .DELTA.spa::Tc.sup.r mutation from 8325-4 .DELTA.spa::Tc.sup.r to strains Newman and Newman clfA::Tn917 using phage 85. Protein A-deficient mutants were used to prevent non-specific interaction with rabbit IgG. Cells from overnight cultures of strains Newman .DELTA.spa::Tc.sup.r and Newman .DELTA.spa::Tc.sup.r clfA::Tn917

were diluted to As60=0.6-1.0 and fixed to glass slides using gluteraldehyde. The slides were then incubated in anti-ClfA region A serum (N2, 1 in 200) followed by fluorescein conjugated swine anti-rabbit serum (Dakopatts, 1 in 40). The cells were studied for fluorescence by microscopy (Nowicki et al., 1984). Newman .DELTA.spa::Tc.sup.r cells fluoresced while Newman .DELTA.spa::Tc.sup.r clfA::Tn917 cells did not (FIG. 9). This confirmed that region A of ClfA is exposed on the cell surface of wild-type Newman and that this ClfA protein is absent in the clumping factor deficient mutant.

Detailed Description Text (27):
A mutant of strain Newman defective in the clumping factor (clfAl::Tn917) and a complemented mutant bearing pCF16 were studied for adherence properties to biomaterials coated in vitro with fibrinogen and to ex vivo biomaterial. A canine arteriovenous shunt has been developed as a model to study plasma protein adsorption onto intravenous catheters from short-term blood-biomaterial exposures and to identify host proteins promoting adhesion of Staphylococcus aureus (Vaudaux et al., 1991).

Detailed Description Text (28):
S. aureus strain Newman adheres strongly (in a concentration dependent fashion) to polymethylmethacrylate (PMMA) coverslips coated in vitro with canine fibrinogen (FIG. 10). In contrast, the fibrinogen receptor mutant was significantly defective (>95%) in its ability to adhere to the canine fibrinogen coated coverslips (FIG. 10). In the ex vivo model, either polyethylene or polyvinyl chloride tubing was exposed to canine blood for 5, 15 or 60 min at a flow rate of 300 ml/min, then flushed in phosphate buffered saline (PBS), cut into 1.5 cm segments and preincubated in 0.5% albumin in PBS to prevent non-specific staphylococcal attachment. Then, each segment was incubated with 4.times.10.sup.6 CFU/ml of [3H]thymidine-labelled S. aureus for 60 min at 37.degree. C. in an in vitro adherence assay. When compared with the wild-type strain Newman, the fibrinogen receptor mutant strain showed a strong decrease (>80%) in attachment to ex vivo polyvinyl chloride and polyethylene tubings (FIG. 11). In addition, strain 8325-4 (which binds poorly to fibrinogen-coated coverslips in vitro and to the ex vivo polymer tubings) showed a significant increase in its ability to adhere to the two different ex vivo polymer tubings when complemented with a plasmid (pCF4) expressing the fibrinogen receptor gene (FIG. 12).

Detailed Description Text (29):
The data shows that fibrinogen is the major plasma protein in a short-term blood material interaction to promote staphylococcal adherence and the possession of the fibrinogen receptor is a major determinant in the ability of S. aureus to adhere to ex vivo biomaterials.

Detailed Description Text (31):
S. aureus strain Newman, the fibrinogen receptor mutant strain of Newman (clfA::Tn917) and a fibrinogen receptor mutant complemented with the clfA+ integrating plasmid pCF16 were compared in a previously described model of experimental endocarditis (Garrison and Freedman, 1970). This rat model investigates the early events in experimental endocarditis with catheter-induced aortic vegetations (Veg). Groups of >/-8 rats were challenged with an inoculum that resulted in 90% of vegetations being colonised by the wild-type organism (ID90). Animals were injected intravenously with the same inocula of Newman clfA and Newman clfA (pCF16). Animals were killed 12 hours after inoculation and quantitative cultures of the blood, spleen and Veg were performed. Table 5 shows the percentage of rats infected.

Detailed Description Text (33):
This model strongly implicates the fibrinogen receptor as an important adhesin in the pathogenesis of S. aureus endocarditis and other cardiovascular infections associated with intravenous catheters, artificial heart valves and intravenous shunts.

Detailed Description Text (35):
1. The fibrinogen binding protein or fragment containing the fibrinogen binding region can be used as a vaccine to protect against human and animal infections caused by S. aureus. For example, the fibrinogen binding protein or fragment containing the fibrinogen binding region can be used as a vaccine to protect ruminants against mastitis caused by S. aureus infections.

Detailed Description Text (36):
2. Polyclonal and monoclonal antibodies raised against the fibrinogen binding protein or a fragment containing the fibrinogen binding domain can be used to immunise passively by intravenous injection against infections caused by S. aureus.

Detailed Description Text (37):
3. The fibrinogen binding protein or an active fragment can be administered locally to block S. aureus from colonising and infecting a wound.

Detailed Description Text (39):
5. The fibrinogen binding protein or an active fragment or antibodies against the fibrinogen binding protein can be used to block adherence of S. aureus to indwelling medical devices such as catheters, replacement heart valves and cardiac assist devices.

Detailed Description Text (40):
6. The fibrinogen binding protein or an active fragment or antibodies against the fibrinogen binding protein can be used in combination with other blocking agents to protect against human and animal infections caused by S. aureus.

Detailed Description Text (41):
7. The fibrinogen binding protein can be used to diagnose bacterial infections caused by S. aureus strains. The fibrinogen binding protein can be immobilised to latex or Sepharose.TM., and sera containing antibodies are allowed to react; agglutination is then measured.

Detailed Description Text (44):
10. Antibodies to the fibrinogen binding protein can be used to diagnose bacterial infections caused by S. aureus strains.

Detailed Description Text (48):
Boden, M. K., and Flock, J. I. (1989). Fibrinogen-binding protein/clumping factor from Staphylococcus aureus. Infect. Immun. 57: 2358-2363.

Detailed Description Text (49):
Boden, M. K., and Flock, J. I. (1992). Evidence for three different fibrinogen binding proteins with unique properties from Staphylococcus aureus strain Newman. Microbiol. Pathogen., 12(4), 289-298.

Detailed Description Text (50):
Boden, M. K., and Flock, J. I. (1994). Cloning and characterization of a gene for a 19 kDa Fibrinogen-binding protein from Staphylococcus aureus. Molec. Microbiol. 12(4), 599-606.

Detailed Description Text (51):
Chhatwal, G. S., Albohn, G. and Blobel, H. (1987). Interaction between fibronectin and purified staphylococcal clumping factor. FEMS Microbiol. Lett. 44, 147-151.

Detailed Description Text (52):

Cheung, A. and Fischetti, V. A. (1990). Role of surface proteins in staphylococcal adherence to catheters in vitro. J. Infect. Dis. 161, 1177-1186.

Detailed Description Text (53):
Cheung, A. L., Kirshnan, N., Jaffe, E. A. and Fischetti, V. A. (1991). Fibrinogen acts as a bridging molecule in the adherence of Staphylococcus aureus to cultured human endothelial cells. J. Clin. Invest. 87, 2236-2245.

Detailed Description Text (54):
Cheung, A. L., Yeaman, M. R. Sullam, P. M., Witt, M. D. and Bayer A. S. (1994). Role of the sar locus of Staphylococcus aureus in induction of endocarditis in rabbits. Infect. Immun. 62, 1719-1725.

Detailed Description Text (56):
Davison, V. E., and Sandford, B. A. (1982). Factors influencing adherence of Staphylococcus aureus to Influenza A virus-infected cell cultures. Infect. Immun. 37:946-955.

Detailed Description Text (57):
Duthie, E. S. (1954). Evidence of two forms of staphylococcal coagulase. J. Gen. Microbiol. 10:427-436.

Detailed Description Text (58):
Espersen, F., Clemmensen, I., and Barkholt, V. (1985). Isolation of Staphylococcus aureus clumping factor. Infect. Immun. 49:700-708.

Detailed Description Text (59):
Garrison, P. K. and Freedman, L. R. (1970). Experimental endocarditis. 1. Staphylococcal endocarditis in rabbits resulting from placement of a polyethylene catheter in the right side of the heart. Yale J. Biol. Med. 42, 394-410.

Detailed Description Text (61):
Hawiger, J. S, Hammond, D. K., Timmons, S. and Budzynski, A. Z. (1978). Interaction of human fibrinogen with staphylococci: presence of a binding region on normal and abnormal fibrinogen variants and fibrinogen derivatives. Blood 51:799-812.

Detailed Description Text (62):
Hawiger, J. S., Timmons, S., Strong, D. D., Cottrell, B. A., Riley, M., and Doolittle, R. F. (1982). Identification of a region of human fibrinogen interacting with staphylococcal clumping factor. Biochemistry 21:1407-1413.

Detailed Description Text (63):
Herrmann, M., Lai, Q. J., Albrecht, R. M., Mosher, D. F. and Proctor, R. A. (1993). Adhesion of Staphylococcus aureus to surface-bound platelets: role of fibrinogen/fibrin and platelet integrins. J. Infect. Dis. 167, 312-322.

Detailed Description Text (64):
Homonylo McGavin, M., Krajewska-Pietrasik, D., Ryden, C. and Hook, M. (1993). Identification of a Staphylococcus aureus extracellular matrix-binding protein with broad specificity. Infect. Immun. 61, 2479-2485.

Detailed Description Text (66):
Kristinsson, K. G. (1989). Adherence of staphylococci to intravascular catheters. J. Med. Microbiol.

28:249-257.

Detailed Description Text (67):
Lantz, M. S., Allen, R. D., Bounelis, P., Switzalski, L. M. and Hook, M. (1990). Bacteriodes gingivalis and Bacteriodes intermedius recognize different sites on human fibrinogen. J. Bacteriol. 172, 716-726.

Detailed Description Text (68):
Lee, C. Y., Buranem, S. L. and Ye, Z-H. (1991). Construction of single copy integration vectors for Staphylococcus aureus. Gene 103:101-105.

Detailed Description Text (69):
McDevitt, D., Vaudaux P. and Foster, T. J. (1992). Genetic evidence that bound coagulase of Staphylococcus aureus is not clumping factor. Infect. Immun. 60:1514-1523.

Detailed Description Text (70):
McDevitt, D., Francois, P., Vaudaux, P. and Foster T. J. (1994). Molecular characterization of the fibrinogen receptor (clumping factor) of Staphylococcus aureus. Molec. Microbiol. 11, 237-248.

Detailed Description Text (73):
Patel, A. H., Nowlan, P. Weavers, E. D. and Foster, T. J. (1987). Virulence of protein A-deficient and alpha toxin-deficient mutants of Staphylococcus aureus isolated by allelic-replacement. Infect. Immun. 55, 3103-3110.

Detailed Description Text (74):
Patti, J. M., Jonsson, H., Guss, B., Switalski, L. M., Wiberg, K., Lindberg, M. and Hook M. (1992). Molecular characterization and expression of a gene encoding a Staphylococcus aureus collagen adhesin. J. Biol. Chem. 267, 4766-772.

Detailed Description Text (76):
Signas, C., Raucci, G., Jonsson, K., Lindgren, P. E., Anantharamaiah, G. M., Hook, M. and Lindberg, M. (1989). Nucleotide sequence of the gene for a fibronectin-binding protein from Staphylococcus aureus: use of this peptide sequence in the synthesis of biologically active peptides. Proc. Natl. Acad. Sci. U.S.A. 86:699-703.

Detailed Description Text (77):
Switalski, L. M. (1976). Isolation and purification of staphylococcal clumping factor. In Staphylococci and staphylococcal diseases. Jeljaszewicz, J. (ed.) Gustav Fischer Verlag, Stuttgart, pp. 413-425.

Detailed Description Text (79):
Usui, Y. (1986). Biochemical properties of fibrinogen binding protein (clumping factor) of the staphylococcal cell surface. 26L. Bakt. Hyg. A262, 287-297.

Detailed Description Text (80):
Vaudaux, P., Pittet, D., Haeberli, A., Huggler, E., Nydegger, U. E., Lew, D. P. and Waldvogel, F. A. (1989). Host factors selectively increase staphylococcal adherence on inserted catheters. A role for fibronectin and fibrinogen or fibrin. J. Infect. Dis. 160, 865-875.

Detailed Description Text (81):
Vaudaux, P., Proctor, R. A., McDevitt, D., Foster, T. J., Lew, D. P., Wabers, H. and S. Cooper. (1991). Use of adherence defective mutants of Staphylococcus aureus (SA) to identify adherence promoting proteins deposited from profusing blood in a canine shunt model. Program Abstr. 31st Intersci. Conf.

Antimicrobiol. Agents Chemother., abst 1068.

Detailed Description Text (82):
Vaudaux, P., Pittet, D., Haeberli, H., Lerch, P. G., Morgenthaler, J. J., Proctor, R. A., Waldvogel, F. A. and Lew, D. P. (1993). Fibronectin is more active than fibrin or fibrinogen in promoting Staphylococcus aureus adherence to inserted intravascular devices. J. Infect. Dis. 167, 633-641.

Detailed Description Paragraph Table (2):
TABLE 2 ______________________________________ Inhibition of clumping with anti-ClfA sera Inhibiting concentration* Sera (micro g) ______________________________________ N2 2.34 N3 2.34 Preimmune N2 >300.00 Preimmune N3 >300.00 C2 >300.00 ______________________________________ *Average of 3 experiments.

Detailed Description Paragraph Table (4):
TABLE 4 ______________________________________ The ability of lysates to block the inhibiting effect of anti-ClfA N2 sera on cell clumping Blocking concentration* Lysate (micro g) ______________________________________ pCF24 1.17 pCF25 >75.00 pCF27 >75.00 pCF28 >75.00 pCF29 >75.00 pCF30 2.34 pCF31 2.34 ______________________________________ *Average of 3 experiments.

[0037] Some specificity domains have a ligand that interacts with a bacterial adhesion receptor including, but not limited to, extracellular fibrinogen binding protein (Efb), collagen binding protein, vitronectin binding protein, laminin binding protein, plasminogen binding protein, thrombospondin binding protein, clumping factor A (ClfA), clumping factor B (ClfB), fibronectin binding protein, coagulase, and extracellular adherence protein. Ligands that have an amino acid sequence corresponding to the C-terminal portion of the gamma-chain of fibrinogen have been shown to competitively inhibit binding of fibrinogen to ClfA, a Staphylococcus aureus adhesion receptor. (McDevvit et al., Eur. J. Biochem., 247:416-424 (1997)). Further, Staphylococcus organisms produce many more adhesion receptors such as Efb, which binds to the alpha chain fibrinogen, ClfB, which interacts with both the .alpha. and .beta. chain of fibrinogen, and Fbe, which binds to the .beta. chain of fibrinogen. (Pei et al., Infect. and Immun. 67:4525 (1999)). Accordingly, preferred specificity domains comprise at least 3 amino acids of a sequence present in a molecule (e.g., fibrinogen) that can bind to a bacterial adhesion receptor

[0017] Some embodiments have antigenic domains that interact with an antibody that has been administered to the subject. For example, an antibody that interacts with an antigenic domain on a ligand/receptor specificity exchanger can be co-administered with the ligand/receptor specificity exchanger. Further, an antibody that interacts with a ligand/receptor specificity exchanger may not normally exist in a subject but the subject has acquired the antibody by introduction of a biologic material (e.g., serum, blood, or tissue). For example, subjects that undergo blood transfusion acquire numerous antibodies, some of which can interact with an antigenic domain of a ligand/receptor specificity exchanger.

[0018] The most desirable antigenic domains

1. 20050026170. 24 Dec 03. 03 Feb 05. Extracellular matrix-binding proteins from Staphylococcus aureus. Patti, Joseph M., et al. 435/6; 530/388.1 530/388.26 C12Q001/68 C07K016/40.

---

☐ 2. 20040254354. 24 Dec 03. 16 Dec 04. Extracellular matrix-binding proteins from Staphylococcus aureus. Patti, Joseph M., et al. 530/382; 435/320.1 435/325 435/69.1 536/23.2 C07K014/75.

---

☐ 3. 20040175731. 12 Nov 03. 09 Sep 04. Methods and products for treating staphylococcal infections. Pier, Gerald B., et al. 435/6; C12Q001/68.

---

☐ 4. 20040019189. 27 Jun 03. 29 Jan 04. Ligand/receptor specificity exchangers that redirect antibodies to receptors on a pathogen. Sallberg, Matti. 530/395; C07K014/31.

---

☐ 5. 20030153022. 05 Nov 02. 14 Aug 03. Monoclonal antibodies to the fibronectin binding protein and method of use in treating or preventing infections. Patti, Joseph M., et al. 435/7.35; G01N033/569.

---

☐ 6. 20030099656. 28 Jan 02. 29 May 03. Monoclonal antibodies to the ClfA protein and method of use in treating or preventing infections. Patti, Joseph M., et al. 424/165.1; 530/388.3 A61K039/40 C07K016/12.

---

☐ 7. 20030087864. 09 Jul 02. 08 May 03. DNA vaccine against staphylococcus aureus. Talbot, Brian, et al. 514/44; A61K048/00.

---

☐ 8. 20020159997. 07 Mar 02. 31 Oct 02. Staphylococcal immunotherapeutics via donor selection and donor stimulation. Patti, Joseph M., et al. 424/142.1; 530/388.15 A61K039/395 C07K016/40.

---

☐ 9. 20010046685. 28 Jun 01. 29 Nov 01. Control for methods for determining platelet count and platelet function. Moskowitz, Keith A., et al. 435/7.21; G01N033/567.

---

☐ 10. 6703025. 31 Aug 99; 09 Mar 04. Multicomponent vaccines. Patti; Joseph M., et al. 424/243.1; 424/184.1 424/190.1 424/193.1 424/203.1 424/234.1 424/244.1 530/350. A61K039/085.

---

☐ 11. 6692739. 31 Aug 99; 17 Feb 04. Staphylococcal immunotherapeutics via donor selection and donor stimulation. Patti; Joseph M., et al. 424/130.1; 424/137.1 424/150.1 424/185.1 530/387.1 530/387.5 530/388.2 530/388.4. A61K039/395.

---

☐ 12. 6660842. 19 Sep 00; 09 Dec 03. Ligand/receptor specificity exchangers that redirect antibodies to receptors on a pathogen. Sallberg; Matti. 530/350; 435/7.1 530/324 530/325 530/326 530/331 530/382 530/807. C07K001/00.

---

☐ 13. 6212562. 28 Mar 97; 03 Apr 01. Criticality and quality of service (QoS) based resource management. Huang; Jiandong. 709/227; 370/468 709/228. G06F015/16 G06F015/17.

---

☐ 14. 4312942. 06 Oct 77; 26 Jan 82. Process for the extraction of microorganisms and diagnostic agents containing them. Blobel; Hans-Georg, et al. 435/7.24; 435/13 435/252.1 435/7.33 435/962 435/963 435/967 436/512 436/828. C12Q001/56 C12R001/08 C12N001/20.

---

☐ 15. 4245039. 08 Jun 76; 13 Jan 81. Stable clumping factor for the identification of fibrinogen and fibrin cleavage products and process for preparing it. Heimburger; Norbert, et al. 435/13; 435/252.1 435/260 435/883. C12Q001/56 C12N001/20 C12R001/445.

---

Generate Collection Print

| Terms | Documents |
|---|---|
| (clfa or clf-a or fnbp or fn-bp or (clumping near2 factor)).clm. | 15 |

Prev Page Next Page